Lung Abnormalities in Systemic Sclerosis Patients through Spirometry, Chest X-Ray, and High-Resolution Computed Tomography Scan

Sumartini Dewi,[1,3] Waliyyuddin Robbani,[2] Iceu Dimas Kulsum[1]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, [2]Faculty of Medicine Universitas Padjadjaran, Indonesia, [3]Immunology Study Center, Faculty of Medicine Universitas Padjadjaran, Indonesia

Abstract

Background: Systemic sclerosis (SSc) is a multisystem autoimmune illness with a wide range of clinical symptoms. The pulmonary organ manifestations frequently occur, but the symptoms are non-specific. Radiological examination and pulmonary function tests (spirometry) are needed to detect lung abnormalities in SSc patients. This study aimed to obtain information about the overview of lung abnormalities in SSc patients through spirometry, chest x-ray, and high-resolution computed tomography (HRCT) scan examination.

Methods: A descriptive qualitative study was conducted on 75 SSc patients registered in Dr. Hasan Sadikin General Hospital Bandung from January 2019 to December 2020. Data were collected with a total sampling method and presented in proportions and percentages.

Results: The majority of subjects were affected by cutaneous 73 (97%), pulmonary 29 (39%), and musculoskeletal 17 (23%) involvement. Spirometry revealed that 43 subjects (57%) had restrictive lung disease, with one false-positive case and two false-negative cases. On a chest x-ray, 45 (60%) of subjects had abnormalities. The majority of subjects were found to have Ground-glass opacities on HRCT scans. Ground-glass opacities were discovered in 46 subjects (82%) and 27 subjects (60%) were identified as having severe fibrosis scores.

Conclusion: According to spirometry results and abnormalities on chest x-ray and HRCT scans, the majority of SSc patients have restrictive lung disease.

Keywords: Chest X-ray, HRCT scan, interstitial lung disease, sclerosis systemic, spirometry

Introduction

Systemic sclerosis (SSc) is a chronic progressive multisystem autoimmune disease with heterogenous clinical manifestations.[1,2] The etiologies are multifactorial, including genetic and environmental.[3] The pathophysiological processes that occur are endothelial dysfunction, autoimmunity and the fibrosis process.[4,5] Based on skin involvement, clinical manifestations, and laboratory examination results, SSc is divided into two subtypes: diffuse cutaneous SSc (dcSSc) and limited cutaneous SSc (lcSSc).[1] SSc can affect all system organs in the body.[6] Pulmonary organ manifestations frequently occur, but the symptoms are non-specific. Symptoms can be fatigue, dry cough, or shortness of breath.[7,8]

Early detection of organ involvement in SSc is essential.[9] Patients diagnosed early and receiving prompt therapy can minimize the possibility of irreversible organ damage.[6] In a study conducted on 953 systemic sclerosis patients, subjects with severe interstitial lung disease (ILD) have a poor prognosis.[8] Another study has shown that one of two main leading causes of death in SSc patients are ILD.[10]

Radiological examination and pulmonary function tests (spirometry) are needed to detect lung abnormalities in SSc patients.[11] Spirometry is more affordable than other modalities because the tools are widely available; however, the obtained results cannot rule out extrapulmonary abnormalities such as skin disorders.[12] A tuberculosis-like appearance often appears on chest X-ray

Correspondence: Dr. Sumartini Dewi, dr., Sp.PD-KR., M.Kes, Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Jalan Pasteur No. 38, Bandung, Indonesia, E-mail: sumartini.dewi@unpad.ac.id

https://doi.org/10.15850/amj.v9n1.2509

examination resulting in misdiagnosis.[13] Chest x-rays also cannot detect early ILD.[14] High-resolution computed tomography (HRCT) scan requires sophisticated equipment and is limited only to a few large hospitals; however, it should still be performed because it is the gold standard for detecting ILD disorders.[15–16]

Research on overview of lung abnormalities on systemic sclerosis patients through spirometry, chest X-ray, and high-resolution computed tomography scan has not been widely studied in Indonesia. This study is expected to add information about the overview of lung abnormalities in SSc patients. The study results are expected to form the basis of future studies and help clinicians be aware of ILD incidence. This study aimed to obtain information about the overview of lung abnormalities in SSc patients through spirometry, chest X-ray, and HRCT scan examination.

Methods

A descriptive qualitative study was conducted on 75 SSc patients obtained from the patient registry in Dr. Hasan Sadikin General Hospital Bandung from January 2019 to December 2020. Data were collected with a total sampling method; proportions and percentages were presented in tables.

The inclusion criteria were spirometry examination, chest X-ray, and HRCT scan data in the systemic sclerosis patient registry. Exclusion criteria were intrapulmonary and extrapulmonary conditions that were not caused by SSc, such as pulmonary tuberculosis or lung tumors and other lung infections.

Variables used in this study were clinical characteristic (age, sex, modified Rodnan skin score, SSc subtype and clinical manifestation) and examination result (spirometry, chest x-ray and HRCT scan).

Age used in this study was the age of subjects when they were admitted to the Rheumatology Clinic Dr. Hasan Sadikin General Hospital, Bandung. Sex consisted of male and female. The modified Rodnan skin score (MRSS) used in this study was the MRSS of subjects when they were admitted to the Rheumatology Clinic Dr. Hasan Sadikin General Hospital, Bandung. SSc subtype consisted of a diffuse and limited type. Clinical manifestations consisted of skin, respiration, musculoskeletal, gastrointestinal, and cardiovascular. Spirometry examination results consisted of restrictive lung disease and were graded based on severity. Chest X-ray consisted of normal and abnormal based on radiologist expertise. Likewise, HRCT scan consisted of normal and abnormal based on radiologist expertise.

This study was approved by the Ethics Committee of Universitas Padjadjaran Bandung, Indonesia (No. 928/UN6.KEP/EC/2020) and obtained the Research Licensing Letter issued by the Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung (No. LB.02.01/X.2.2.1/2271/2021).

Results

The study result showed that the majority of subjects were female (97%). The mean age of the subjects was 39.08±13.52 years. Furthermore, the median MRSS score of the subjects was 15 (0–39). Most of the subjects had a diffuse type of SSc of 63%. The most common clinical manifestations were skin disorders 97%, respiratory disorders 39%, and musculoskeletal disorders 23% (Table 1).

The spirometry examination showed that most subjects had restrictive lung disease (57%) (Table 2). From chest X-ray examinations, 30 subjects (40%) had normal results and 45 (60%) had abnormal results (Table 3).

There were 19 subjects (25%) of the 75 subjects who did not undergo an HRCT scan. Only 56 subjects (75%) underwent HRCT scan examination. The most common lung abnormality based on HRCT scan was Ground-glass opacities (GGO) in 46 subjects (82%) (Table 4).

There were 30 subjects (40%) with fibrosis scores that were not calculated, while most of the subjects with a score that was calculated (27 subjects, 60%) had severe pulmonary fibrosis (Table 5).

Discussion

This study showed a significant difference in gender among all patients at the Rheumatology Clinic Dr. Hasan Sadikin General Hospital, Bandung. The ratio of male and female was 73 and 2. This is consistent with a cohort study conducted by EULAR Scleroderma Trials and Research (EUSTAR) in 2011 in Europe, where the incidence of SSc in women was greater than that of men.[17]

Based on the subtype, diffuse SSc is the most common, this finding is appropriate with literature that states the diffuse type of SSc is the most common subtype of SSc.[5]

There were 73 subjects (97%) who had skin disorders, 29 subjects (39%) with respiratory

Table 1 Clinical Characteristic of Systemic Sclerosis Patients

Characteristics	Total (n=75)
	n (%)
Age on average (years)	39.08±13.52
Gender	
Female	73 (97)
Male	2 (3)
MRSS score median	15 (0–39)
SSc subtype	
Diffuse	47 (63)
Limited	28 (37)
Clinical manifestation	
Skin	73 (97)
Skin stiffness	67 (89)
Raynaud's phenomenon	62 (83)
Sclerodactyly	60 (80)
Fish mouth	44 (59)
Salt and pepper appearance	35 (47)
Digital scar	33 (44)
Telangiectasia	29 (39)
Sausage fingers	25 (33)
Ulkus digity	23 (31)
Post inflammation hyperpigmentation	6 (8)
Respiration	29 (39)
Interstitial lung disease	20 (27)
Dyspnea	18 (24)
Dry cough	11 (15)
Pulmonary hypertension	7 (9)
Pleural effusion	1 (1)
Musculoskeletal	17 (23)
Arthralgia	15 (20)
Joint stiffness	5 (7)
Myopathy	1 (1)
Gastrointestinal	7 (9)
Dry mouth	4 (5)
Nausea	2 (3)
Decreased body weight	2 (3)
Bloating	2 (3)
Vomiting	1 (1)
Esophageal dysmotility	1 (1)
Cardiovascular	4 (5)
Chest pain	1 (1)
Palpitation	1 (1)
Constrictive pericarditis	1 (1)
Congestive heart failure	1 (1)
N/A	2 (3)

Note: Most of the subjects had overlapping clinical examinations, MRSS=modified Rodnan skin score

Table 2 Spirometry Results of Systemic Sclerosis Patients

Spirometry Results	Total (n=75)
	n (%)
Normal	3 (4)
Restrictive lung diseases	43 (57)
Mild	19 (25)
Moderate	24 (32)
Severe	0
Very severe	0
N/A	29 (39)

Note: N/A= not available; Not all subjects undergo spirometry examination

disorders, and 17 subjects (23%) with musculoskeletal disorders. This is appropriate with the literature that states skin disorders, respiratory disorders, and musculoskeletal disorders are the most common manifestations in SSc subjects.[6]

Based on pulmonary function tests (spirometry), 43 subjects (57%) had restrictive lung abnormalities. One subject had normal spirometry results with abnormal chest HRCT scan result, which was mild pulmonary fibrosis. Two subjects had mild restrictive spirometry examination results with normal chest scan HRCT results. Suliman et al.[18] in their study at the Zürich University Hospital, state that spirometry is only able to detect 59 of 102 SSc-ILD patients. Errors in the detection of lung abnormalities in these SSc patients are partly due to the low level of sensitivity and the limitations of the spirometry device, which cannot distinguish the cause of the restriction whether it is due to lung abnormalities, or from the stiffness of the chest and abdominal skin that is common in SSc patients.[18] In this study, some subjects had mild restrictive spirometry results, but their chest scan HRCT results were normal. These subjects had skin disorders in the form of diffuse cuticle sclerosis that affects the chest wall and abdomen. This suggests that spirometry has limitations and can show false positive or false negative results, and can lead to false diagnosis if used as the primary modality in SSc-ILD detection.

On chest X-ray, 45 subjects (60%) had abnormal results, and 30 subjects (40%) had normal results. In the group of subjects with normal chest X-ray, 16 subjects (21%) had abnormal HRCT scan results. In the group of subjects with normal chest X-ray but abnormal HRCT scan results, 9 subjects (12%) had

Table 3 Chest X-Ray Results of Systemic Sclerosis Patients

Variables	Total (n=75)	
	n (%)	Proportion
Chest X-ray results[b]		
Normal pattern	30 (40)	0.400
Abnormal	45 (60)	0.600
Cardiomegaly	22 (29)	0.293
Bronchopneumonia	9 (12)	0.120
Suggestive ILD	8 (10)	0.106
Bronchitis	7 (9)	0.093
Pleural effusion	6 (8)	0.080
Aortic atherosclerosis	6 (8)	0.080
Tuberculosis	4 (5)	0.053
Pneumonia	3 (4)	0.040

Note: Some subjects have more than one abnormality on chest X-ray, ILD=interstitial lung disease

Table 4 HRCT Scan Results of the Systemic Sclerosis Patients

HRCT Scan Results	Total (n=56)	
	n (%)	Proportion
Ground glass opacities	46 (82)	46 (82)
Bronchiectasis	35 (62)	35 (62)
Irregular pleural margins	13 (23)	13 (23)
Honeycombing	8 (14)	8 (14)
Subpleural cyst	6 (11)	6 (11)
Subpleural lines	2 (3)	2 (3)

Note: Not all subjects undergo HRCT scan examination and most of the subjects has more than one lung abnormality based on HRCT scan examination, HRCT=high-resolution computed tomography

Table 5 Fibrosis Severity Score Based on HRCT Scan Examination of Systemic Sclerosis Patients

Variables	Total (n=45)	
	n (%)	Proportion
Normal	2 (4)	0.044
Mild	7 (15)	0.155
Moderate	9 (20)	0.200
Severe	27 (60)	0.600

Note: Not all HRCT scan results are calculated for the degree of pulmonary fibrosis

restrictive spirometry results; restrictive mild in 4 subjects (5%) and moderate restrictive in 5 subjects (7%). A study conducted by Morales-Cárdenas et al.[19] mentions that the HRCT scan can detect SSc-ILD at the disease onset. This suggests that chest X-ray examination is not accurate in detecting SSc-ILD at the onset of the disease. However, the spirometry examination as an additional modality can increase accuracy in SSc-ILD diagnosis, especially in health facilities that do not have access to HRCT chest scans or at SSc patients who cannot perform HRCT thoracic scans.[20]

Four subjects (5%) had a chest X-ray image of active TB in this study. According to a study conducted by Agrawal et al.[13] in 2019, the radiological features of ILD are similar to pulmonary tuberculosis, so misdiagnosis often occurs. When a chest HRCT scan is performed on a subject who has a chest X-ray in the form of active TB, there is no visible

infiltrate characteristic of TB infection. This suggests that chest X-rays cannot differentiate infiltrates due to SSc fibrosis or from TB infection and may cause errors in the diagnosis of pulmonary abnormalities in SSc patients.

On the chest HRCT scan, the most common type of lung lesion in SSc patients with pulmonary abnormalities was the type of GGO lesion, which were 46 subjects (82%). This is consistent with the study conducted by Sambataro et al.[21] in 2020, which states that the type of GGO lesions often appears on the chest HRCT scan of SSc patients with pulmonary abnormalities.

This study is a qualitative descriptive study that evaluates data from spirometry, chest X-ray, and HRCT scan recorded in the systemic sclerosis patient registry; however, not all subjects undergo chest X-ray or chest HRCT examination, so that not all results are recorded.

The subject's condition when performing spirometry examination was not recorded in the systemic sclerosis patient registry. This can lead to bias since several intrapulmonary and extrapulmonary conditions do not result from SSc, such as skin and muscle stiffness at the chest and abdominal wall, pregnancy, and spine abnormalities affecting chest expansion.[12] All data taken are only based on the sclerosis systemic patient registry, which may cause errors in data input actions. Data errors have been minimized by cross-checking with data from the Respirology Division for spirometry results and Radiology Department for chest X-ray and HRCT scan results. Some subjects did not undergo supporting examinations at hospital, so the incomplete data could not be searched in the patient's medical record.

In conclusion, most SSc patients have restrictive lung disease based on spirometry examination, and abnormality based on chest X-ray and HRCT scan examination. The HRCT scan examination remains the gold standard in a suspected interstitial lung disease case. Furthermore, spirometry and chest X-ray cannot detect early interstitial lung disease. Spirometry cannot distinguish the causes of restrictive lung disease resulting from SSc or skin abnormalities in SSc patients. Further study is needed to explore the lung abnormalities in Systemic sclerosis using various modalities.

Funding

Internal Research Grant from Universitas Padjadjaran.

References

1. Kasper D, Fauci A, Longo D, Hauser S, Jameson J, Loscalzo J. Harrison's principles of internal medicine. 19th ed. New York: McGraw-Hill; 2015. p. 2154–5.
2. Dewi S, Isbagio H, Purwaningsih EH, Kertia N, Setiabudy R, Setiati S. A double-blind, randomized controlled trial of ciplukan (physalis angulata Linn) extract on skin fibrosis, inflammatory, immunology, and fibrosis biomarkers in scleroderma patients. Acta Med Indones. 2019;51(4):303–10.
3. Fett N. Scleroderma: nomenclature, etiology, pathogenesis, prognosis, and treatments: facts and controversies. Clin Dermatol. 2013;31(4):432–7.
4. Kumar V, Abbas A, Aster J. Robbins and Cotran Pathologic Basis of Disease. 9th ed. Philadelphia: Elsevier; 2014.
5. Padmandani WPA, Dewi S, Hamijoyo L. Correlation between serum C-reactive protein (CRP) and soluble Cd40 ligand (sCD40L) with disease activity by modified rodnan skin score (mRSS) in systemic sclerosis patients in Indonesia. Ina J Rheum. 2018;10(2). [Cited 2021 January 28]. Available from: https://journalrheumatology.or.id/index.php/ijr/article/view/100.
6. Budiman AM, Dewi S, Prananta MS. Clinical manifestation and laboratory finding of sclerosis systemic patient in Dr. Hasan Sadikin General Hospital Bandung: a descriptive quantitative study. Ina J Rheum. 2018;10(1):15–9.
7. Hant FN, Herpel LB, Silver RM. Pulmonary manifestations of scleroderma and mixed connective tissue disease. Clin Chest Med. 2010;31(3):433–49.
8. Hassoun PM. Lung involvement in systemic sclerosis. Presse Med. 2011;40(1 Pt 2):e3–17.
9. Khanna D. Diagnosis and treatment of systemic and localized scleroderma. Expert Rev Dermatol. 2011;6(3):287–302.
10. Bussone G, Mouthon L. Interstitial lung disease in systemic sclerosis. Autoimmun Rev. 2011;10(5):248–55.
11. Solomon JJ, Olson AL, Fischer A, Bull T, Brown KK, Raghu G. Scleroderma lung disease. Eur Respir Rev. 2013;22(127):6–19.
12. Wong CJ, Hamlin NP, editors. The perioperative medicine consult handbook. New York: Springer; 2013.
13. Agrawal N, Dave L, Shrivastava N, Sharma

P. Study of clinico-radiological profile of interstitial lung disease patients attending CRGH Ujjain. Int J Med Sci Diagnosis Res. 2019;3(12):25–30.
14. Vizioli L, Ciccarese F, Forti P, Chiesa AM, Giovagnoli M, Mughetti M, et al. Integrated use of lung ultrasound and chest X-ray in the detection of interstitial lung disease. Respiration. 2017;93(1):15–22.
15. Varga J, Denton CP, Wigley FM, Allanore Y, Kuwana M, editors. Scleroderma: from pathogenesis to comprehensive management. 2nd ed. Cham, Switzerland: Springer International Publishing; 2017.
16. Assayag D, Kaduri S, Hudson M, Hirsch A, Baron M. High resolution computed tomography scoring systems for evaluating interstitial lung disease in systemic sclerosis patients. Rheumatology. 2012;(S1):003.
17. Meier FMP, Frommer KW, Dinser R, Walker UA, Czirjak L, Denton CP, et al. Update on the profile of the EUSTAR cohort: an analysis of the EULAR Scleroderma Trials and Research group database. Ann Rheum Dis. 2012;71(8):1355–60.
18. Suliman YA, Dobrota R, Huscher D, Nguyen-Kim TDL, Maurer B, Jordan S, et al. Pulmonary function tests: high rate of false-negative results in the early detection and screening of scleroderma-related interstitial lung disease. Arthritis Rheumatol. 2015;67(12):3256–61.
19. Morales-Cárdenas A, Pérez-Madrid C, Arias L, Ojeda P, Mahecha MP, Rojas-Villarraga A, et al. Pulmonary involvement in systemic sclerosis. Autoimmun Rev. 2016;15(11):1094–108.
20. Yani H, Dewi S, Rahmadi AR. Correlation between serum krebs von den lungen-6 levels with forced vital capacity and modified rodnan skin score of patients with restrictive lung disease in diffuse-type systemic sclerosis. Ina J Rheum. 2019;11(2):145–7.
21. Sambataro D, Sambataro G, Pignataro F, Maglione W, Malatino L, Vancheri C, et al. Quantification of ground glass opacities can be useful to describe disease activity in systemic sclerosis. Diagnostics (Basel). 2020;10(4):225.